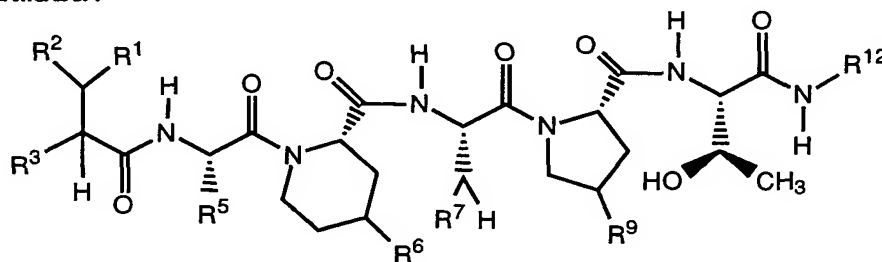


PIPECOLIC ACID DERIVATIVES OF PROLINE THREONINE
AMIDES USEFUL FOR THE TREATMENT OF RHEUMATOID
ARTHRITIS

5

ABSTRACT

Non-peptidic compounds characterized by containing a segment condensed from pipecolic acid, aspartic acid, proline and threonine, or derivatives thereof, are
 10 useful to treat autoimmune diseases and inflammatory conditions. Compounds of particular interest are those of the formula:



wherein R¹ is phenyl or cyclohexyl; wherein R² is hydrido or
 15 methyl; wherein R³ is selected from hydrido, hydroxy, acetylamino, acetyl(Lys/Tyr/Thr)NH-, propionylamino and benzyloxycarbonylamino; wherein R⁵ is selected from isopropyl, isobutyl, n-propyl, n-butyl, aminopropyl, aminobutyl, phenyl, benzyl, hydroxyphenyl, hydroxybenzyl,
 20 morpholinocarbonylethyl, morpholinocarbonylpropyl, piperazinocarbonylethyl, piperazinocarbonylpropyl, pyridinylcarbonylethyl, pyridinylcarbonylpropyl, oxazolylcarbonylethyl, oxazolylcarbonylpropyl, azepinylcarbonylethyl and azepinylcarbonylethyl; wherein R⁶
 25 is selected from hydrido, methyl, hydroxy, methoxy, phenyl and aminocarbonyl; wherein R⁷ is carboxyl or methylthiomethyl; wherein R⁹ is selected from hydrido, hydroxy, methoxy and phenyl; wherein R¹² is selected from methyl, ethyl, propyl, butyl, isobutyl, -CH(iBu)CH₂OH and
 30 -CH(iBu)CONH₂; or a pharmaceutically-acceptable amide, ester or salt thereof. A disease state of particular interest for use of the compounds would be rheumatoid arthritis.